

# Evaluation of clinical extrapolation, safety and feasibility for the development of trogocytosis-controlled cleavable CAR-T cells

# S1-226106

Atsutaka Minagawa, M.D., Ph.D.  
Deputy Director, Kyoto University Center for iPS Research



## Vision

We aim to develop CAR-T cell products that can increase response rates and suppress post-treatment recurrence by controlling trogocytosis—a phenomenon involving the intercellular transfer of proteins driven by the immune response.

All CAR-T cell products currently in clinical trials induce strong trogocytosis between CAR-T cells and cancer cells upon administration. Furthermore, it is known that the reduction in anti-tumor antigen expression in cancer cells caused by trogocytosis leads to treatment resistance through immune evasion. In this project, we will clinically demonstrate that CAR-T cell therapies that are less likely to miss cancer cells can be developed by suppressing trogocytosis using Cleavable-CAR, and we will develop this into a platform technology applicable to CAR-T therapy across various modalities.

## Marketability

We are advancing the development of a cleavable CAR-T cell therapy targeting CADM-1 in adult T-cell leukemia (ATL). ATL is a disease with a poor prognosis for which no effective standard treatment has yet been established, and for which there is a significant unmet medical need.

ATL alone accounts for approximately 800 new cases per year in Japan; by expanding the range of conditions it treats, a market worth over 100 billion yen annually exists. By demonstrating the therapeutic efficacy of ATL, we will enhance its market value as a platform technology.

## Innovation

Cleavable-CAR is a novel mechanism whereby the CAR receptor undergoes cleavage upon antigen binding, thereby inhibiting trogocytosis. Due to its extremely simple structure, it is compatible with CARs featuring a variety of ScFvs and can be easily combined with other technologies.

## Partnering

### 【 Expected partners 】

• Pharmaceuticals • Medical institute •  
• Biotech/Drug Discovery Service • CMO/CDMO/CRO/SMO

### 【 Expectation 】

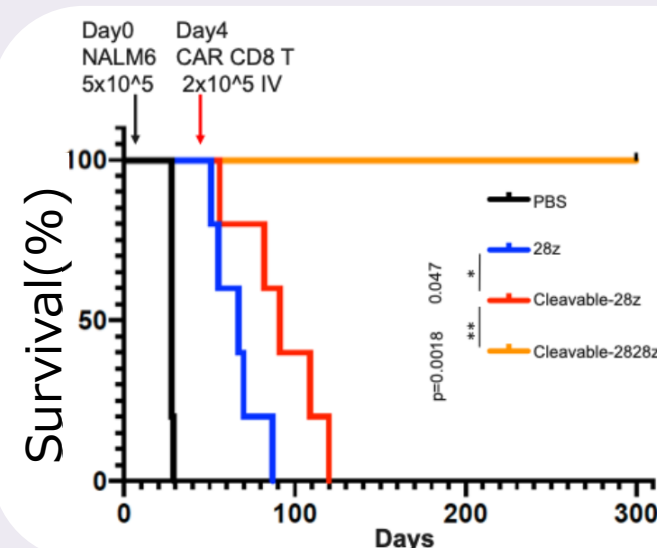
• Manufacture of investigational medicinal products, conduct of clinical trials, analysis of clinical samples, identification of potential licensees,

## Research Outline

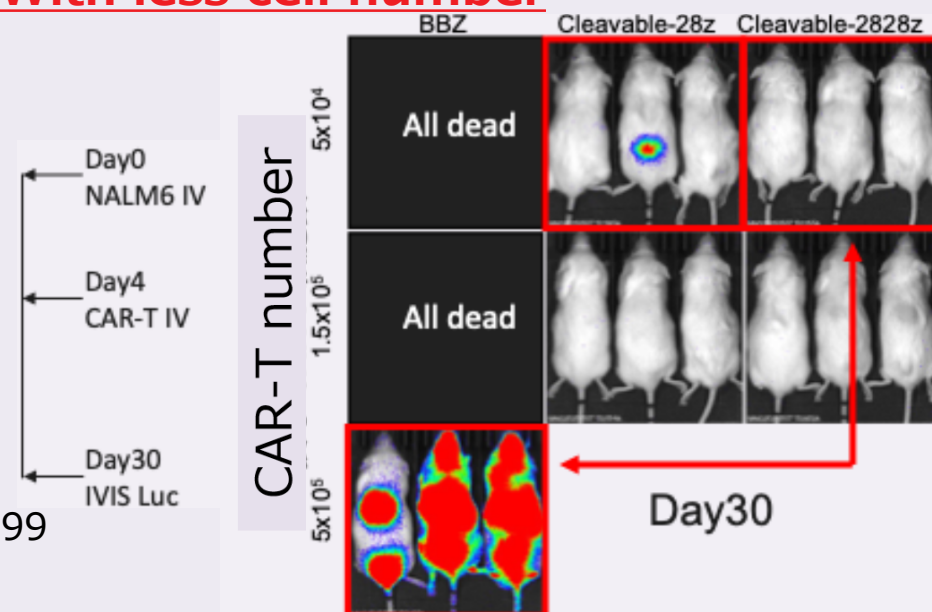
Key Words: #CAR-T, #Trogocytosis

A known challenge with current CAR-T cell therapy is antigen loss due to trogocytosis and the resulting early relapse. The relapse rate following CAR-T treatment has been reported to be 30–50%, highlighting the need for improvement. In Cleavable-CAR, which incorporates an amino acid sequence near the CAR cell membrane that is cleaved following antigen binding, trogocytosis is suppressed, leading to enhanced therapeutic efficacy. The number of cells required to achieve equivalent therapeutic efficacy can also be reduced, and its application in various forms of CAR therapy is anticipated.

## Strong therapeutic effect



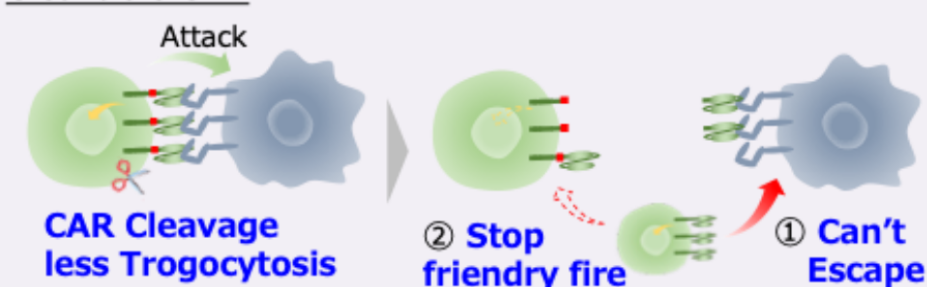
## With less cell number



### Trogocytosis



### Cleavable CAR



Minagawa, et al. Research square Jan 2025 10.21203/rs.3.rs-5274199

Patent : PCT/JP2023/026123